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# Factors of increase in serum triglyceride-rich lipoproteins in uremic rats

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**Factors of increase in serum triglyceride-rich lipoproteins in uremic rats.** The possible mechanisms of the increase in serum triglycerides (TG) and TG-rich lipoproteins were studied in chronically uremic (U) rats by comparison with either ad-lib fed control (C) rats or diet-restricted (DR), sham-operated pair-fed control rats. A first series of animals was studied in the fed state and a second series after a 16-hr fast. In U animals the concentration of serum TG and TG-rich particles was lower than that of C rats in the fed state but significantly higher than that of C and DR rats after a 16-hr fast. Serum glucose and lactate concentrations in the fed or fasted state were unchanged by uremia. Serum insulin concentration was significantly decreased in U rats as compared to C and DR rats in both series. The fast did not increase the concentration of serum nonesterified fatty acids (NEFA) in U or DR animals to the same extent as in C rats, whereas the serum concentration of β-hydroxybutyrate (BOB), which was higher than that of C rats in the fed state, was significantly lower after a 16-hr fast. In U animals, as compared to control rats of either series, a significant decrease of epididymal lipoprotein lipase (LPL) activity was observed during both nutritional states when expressing the enzymic activity per number of cells. In conclusion, our data provide evidence against hepatic overproduction of TG-rich lipoproteins in rats with chronic renal failure and strongly point to an LPL-mediated defect of their peripheral catabolism, probably related to the insulin deficiency state.

**Les facteurs de l'augmentation dans lipoprotéines sériques riches en triglycérides chez des rats en insuffisance rénale.** Les mécanismes possibles de l'augmentation des triglycérides (TG) sériques et des lipoprotéines riches en TG ont été étudiés chez des rats en insuffisance rénale chronique (U) en comparaison avec des rats témoins, soit nourris ad libitum (C), soit recevant la même quantité de nourriture que les rats U et ayant subi un simulacre d'opération (DR). Les animaux d'une première série ont été analysés à l'état nourri et ceux d'une seconde série après un jeûne de 16 hr. Chez les rats U la concentration sérique des TG et des particules riches en TG est plus faible que celle des rats C à l'état nourri alors qu'elle est significativement plus élevée que celle des rats C et DR après un jeûne de 16 hr. Les concentrations sériques de glucose et de lactate ne sont pas modifiées par l'urémie chronique quel que soit l'état de jeûne de l'étude. En revanche, les concentrations sériques d'insuline sont significativement diminuées chez les rats U par rapport aux rats C et DR dans les deux séries expérimentales. La réponse au jeûne montre que les acides gras non estérifiés n'augmentent pas autant chez les rats U et DR que chez les rats C. Chez les rats U, la concentration sérique de β-hydroxybutyrate est plus élevée que celle des rats C à l'état nourri alors qu'elle est significativement plus faible après un jeûne de 16 hr. Enfin, chez les animaux U, il existe une diminution significative de l'activité de la lipoprotéine lipase du tissu adipeux épididymaire (LPL) dans les deux états nutritionnels par rapport aux deux groupes témoins, quand l'activité est exprimée par cellule. En conclusion, nos données permettent d'éliminer une surproduction hépatique de lipoprotéines riches en TG chez les rats en insuffisance rénale chronique pour expliquer leur hypertriglycéridémie, et elles démontrent que la cause en est une diminution du catabolisme périphérique de ces lipoprotéines en raison d'un déficit en LPL, probablement en rapport avec un état de déficience chronique en insuline.

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Chronic renal failure in humans is associated with an increase in serum total triglyceride (TG) and very low density lipoprotein (VLDL) concentration [1–3]. The disturbed metabolism of TG-rich lipoproteins has been generally attributed to a decrease in several enzyme activities such as lipoprotein lipase (LPL) according to some authors, hepatic lipase (HL) for others [4–11], and also lecithin cholesterol acyl transferase [12, 13]. However, there still exists some controversy concerning the depression of both lipase activities in uremic patients. The distinction between LPL and HL activities, respectively, in serum is difficult to verify with data. Furthermore, in vitro methods using human tissue such as muscle cells or adipocytes for the exploration of LPL activity may yield equivocal results, depending essentially on the mode of expression of enzyme activity. When reviewing the literature it becomes apparent that only those investigators who expressed adipose tissue LPL activity in the human per number of adipocytes have been able to demonstrate a significant decrease in uremic patients as compared to healthy subjects [4, 5]. However, the authors who expressed adipose tissue LPL activity in terms of grams of tissue weight did not find a decrease in patients with chronic renal failure and therefore concluded that this enzyme played only a minor role, if any, in the disturbed catabolism of TG-rich particles in uremic humans.

The first purpose of the present experimental study in rats was to investigate whether a decrease in adipocyte LPL activity existed during chronic renal failure and thus whether this enzyme played an important role in the decreased metabolism of TG-rich particles in this setting. The second purpose of the study was to explore the possible contribution of disturbed energy metabolism and altered hormone status to the anomalies of TG metabolism of chronic renal failure.

## Methods

### *Animal model*

Male Wistar AF rats, weighing 180 to 200 g, were randomly allocated to three groups (control rats, uremic rats, or

nonuremic, sham-operated and pair-fed rats) within two experimental series. The first series was studied in the fed state (1 hr fast) and the second series after a 16-hr fast.

Control (C) rats did not undergo a surgical intervention and had free access to diet. Rats rendered uremic (U) by cortical electrocoagulation of one kidney and contralateral nephrectomy according to a previously described technique [14] had also no dietary restriction. Sham-operated, diet-restricted (DR) rats were pair-fed with their respective uremic littermates. All animals were housed in lighted individual cages between 8 AM and 6 PM. They had free access to water and were fed the standard diet of the laboratory containing proteins 24%, cellulose 6.5%, lipids 4.5%, glucides 45%, vitamin D 200 IU, minerals 8% (with Ca 1.5% and P 0.95%), and water 12% (Pietrement Laboratoire, Colombes, France).

The animals were observed during a time period of 35 days after nephrectomy. During this experimental period the food intake (g/24 hr) was 23.1 ± 1.2 and 22.5 ± 0.8 (mean ± SEM) for U and DR rats of series 1 and 2, respectively. Despite a comparable daily food intake, the mean body weight gain during the experimental time period was significantly higher in DR rats than in U rats (105.5 ± 4.7 vs. 68.4 ± 9.4 g for series 1 and 88.4 ± 6.6 vs. 44.2 ± 8.8 g for series 2).

At the end of the experimental period, the rats were decapitated by guillotine, without anesthesia. Blood and tissue sampling was always done between 8 and 9 AM. Blood was sampled in the absence of anticoagulant and sera were conserved at −50°C for subsequent analysis. Mean serum creatinine concentration was comparable in uremic rats of series 1 and 2 at the end of the experimental period and was two to three times higher than that of control rats (221.8 ± 19 vs. 82.2 ± 2.6 μmoles/liter and 191 ± 18.2 vs. 85. ± 2.0 μmoles/liter for series 1 and 2, respectively).

Epididymal adipose tissue was removed rapidly after sacrifice. One aliquot was transferred to Bouin's fixation fluid for cell counting under the light microscope. A second aliquot was immediately frozen in liquid nitrogen and then conserved at −50°C for subsequent analysis of LPL activity after tissue delipidation with acetone and ether (AE-LPL).

### *Biochemical analyses*

*Lipoprotein lipase assay.* Lipoprotein lipase activity was assayed in acetone-ether preparations performed according to the micromethod of Nilsson-Ehle, Tornqvist, and Belfrage [15]. Enzymatic activity was calculated according to the formula of Nilsson-Ehle and Schotz [16] and expressed as milliunits per gram of adipose tissue wet weight, or nanounits per number of cells. Interassay precision as tested by the postheparin serum assay was of 8.4% (CV) for a mean activity of 475.9 mU/ml of serum ($N = 16$).

*Epididymal fat cell count.* Fixed specimens of epididymal adipose tissue were dehydrated, embedded in wax, sectioned (5-μm thick), then dewaxed, rehydrated, and stained with hematin-eosine-safran. Fields of representatively sized cells were photographed at known magnification. The number of cells counted on a 10 × 18 cm photograph (final magnification ×200) will be referred to as the number of cells observed per high power field.

Considering the number of cells and magnification, we calculated cell diameter as indicated by Ashwell et al [17] and then the number of cells per adipose tissue weight considering the density of adipose tissue to be similar in the three animal groups (d = 0.88). Adipose tissue density was measured in preliminary studies using methanol-water solutions of varying density. No significant difference was found between the tissues of the three animal groups. However, it must be noted that this method may not be sensitive enough to detect variations of tissue density less than 0.01.

*Isolation of serum lipoproteins.* The lipoproteins were isolated by flotation [18] at d = 1006 for VLDL or TG-rich particles and d = 1006–1063 for LDL, in an ultracentrifuge using a 50.3 Ti Rotor (model L8-55, Beckman Instruments, Inc., Fullerton, California, USA).

*Quantitation of hormones.* Serum insulin was determined using an INSIK-3 kit (Sorin Laboratory, Biomedica S.p.A., Italy), characterized by a cross-reaction of 90% with rat insulin for a 50% inhibition of tracer binding and a cross-reaction of 7% with proinsulin. This assay was sensitive (2.5 mU/liter) and reproducible (intraseries CV of 5% for 26 mU/liter). Serum glucagon was determined using a glucagon kit (Hypolab, ref. 1904, Coinsins, Switzerland). The sensitivity of the assay was 60 ng/liter and intraseries CV, 12% for 250 ng/liter.

*Serum creatinine, triglycerides, and energy substrates.* Creatinine (kinetic method of Jaffé, Roche Diagnostica, ref. 1421), triglycerides (enzymatic method, Boehringer ref. 24052), glucose (Glucibiotrol, Biotrol, ref. 101538), lactate (lactates UV-system, Boehringer, ref. 149993), and β-hydroxybutyrate (BOB) using the enzymatic method of Li et al [19] were quantitated on a centrifugal analyzer (Cobas Bio, Roche, France). Nonesterified fatty acids (NEFA) extracted from serum by chloroform were determined according to Duncombe's method [20].

### *Statistical analyses and expression of results*

The comparison between two groups of independent values was made using Student's *t* test unless the latter was rejected by the F test. In that case, the nonparametric U test of Mann and Whitney was used.

Results have been expressed in terms of mean values ± 1 SEM.

## Results

### *Effect of chronic uremia versus chronic dietary restriction on serum triglyceride concentration and role of acute fast*

Table 1 shows that in the fed state, the concentration of serum TG and serum TG-rich particles of U and DR rats was lower than that of C rats. After a 16-hr fast, U rats had a significantly higher mean serum total TG and VLDL-TG concentration than control rats (C or DR).

In the two experimental series, U rats had a higher serum LDL-TG concentration than C or DR rats after a 1-hr fast which was even more pronounced after a 16-hr fast.

### *Effect of chronic uremia versus chronic dietary restriction on serum energetic substrate concentrations and role of acute fast*

Table 2 shows that U rats had a normal serum glucose concentration in the fed state as well as after a 16-hr fast, by comparison with C rats. Mean serum glucose concentration of

**Table 1.** Total serum and lipoprotein triglyceride concentrations

| Parameters | Fasting time | Control rats ($N$ = 8) | DR rats ($N$ = 8) | Uremic rats ($N$ = 8) |
|---|---|---|---|---|
| Serum TG conc, *mmoles/liter* | 1 hr | 2.24 ± 0.17 | 1.80 ± 0.14 | 1.79 ± 0.11[b] |
| Serum TG-rich particles conc, *mmoles/liter* | 1 hr | 1.97 ± 0.10 | 1.55 ± 0.09[a] | 1.49 ± 0.05[b] |
| Serum LDL-TG conc, *mmoles/liter* | 1 hr | 0.152 ± 0.013 | 0.146 ± 0.032 | 0.195 ± 0.020 |
| Serum TG conc, *mmoles/liter* | 16 hr | 1.01 ± 0.07 | 1.22 ± 0.08 | 1.60 ± 0.19[b,c] |
| Serum VLDL-TG conc, *mmoles/liter* | 16 hr | 0.86 ± 0.02 | 1.04 ± 0.036[a] | 1.29 ± 0.069[b,c] |
| Serum LDL-TG conc, *mmoles/liter* | 16 hr | 0.078 ± 0.019 | 0.123 ± 0.026 | 0.244 ± 0.066[b] |

Abbreviations: DR, diet-restricted; TG, triglycerides; LDL, low density lipoproteins; VLDL, very low density lipoprotein.
[a] $P < 0.05$ or less for DR vs. Controls.
[b] $P < 0.05$ or less for Uremics vs. Controls.
[c] $P < 0.05$ or less for Uremics vs. DR.
In all other instances, $P$ is not significant.

**Table 2.** Serum energetic substrate concentrations

| Parameters | Fasting time | Control rats ($N$ = 8) | DR rats ($N$ = 8) | Uremic rats ($N$ = 8) |
|---|---|---|---|---|
| Serum glucose conc, *mmoles/liter* | 1hr | 7.52 ± 0.23 | 7.24 ± 0.18 | 7.94 ± 0.19[c] |
| | 16 hr | 7.47 ± 0.28 | 8.08 ± 0.29 | 6.76 ± 0.27[c] |
| Serum lactate conc, *mmoles/liter* | 1 hr | 5.30 ± 0.50 | 5.30 ± 0.20 | 5.90 ± 0.60 |
| | 16 hr | 5.42 ± 0.54 | 5.68 ± 0.52 | 5.25 ± 0.84 |
| Serum NEFA conc, *μmoles/liter* | 1 hr | 248 ± 38 | 365 ± 45 | 266 ± 34 |
| | 16 hr | 716 ± 57 | 380 ± 59[a] | 407 ± 38[b] |
| Serum BOB conc, *mmoles/liter* | 1 hr | 1.21 ± 0.05 | 1.40 ± 0.11 | 1.64 ± 0.11[b] |
| | 16 hr | 2.23 ± 0.25 | 0.66 ± 0.10[a] | 1.90 ± 0.22[c] |

Abbreviations: DR, diet-restricted; TG, triglycerides; NEFA, nonesterified fatty acids; BOB, β-hydroxybutyrate.
[a] $P < 0.05$ or less for DR vs. Controls.
[b] $P < 0.05$ or less for Uremics vs. Controls.
[c] $P < 0.05$ or less for Uremics vs. DR.
In all other instances, $P$ is not significant.

DR rats was also not different from that of C rats. As to serum lactate concentration, no change was induced by the uremic state or diet restriction, neither in the fed state nor after a 16-hr fast. Serum NEFA concentration was similar in C, DR, and U rats in the fed state. However, after a 16-hr fast, DR and U rats had a significantly lower mean serum NEFA concentration than C rats (Table 2). Serum BOB concentration was significantly increased in U rats by comparison with C or DR rats in the fed state, while after a 16-hr fast, U rats had a serum BOB concentration significantly lower than C rats, but significantly higher than DR rats.

### *Effect of chronic uremia versus chronic dietary restriction on circulating insulin and glucagon and role of acute fast*

Table 3 shows a striking decrease in serum insulin concentration in U rats in the fed state as well as after a 16-hr fast by comparison with C or DR rats. Circulating glucagon concentration was higher in U rats than in C and DR rats (Table 3). A strong correlation was found between serum glucagon and serum creatinine values in U rats of the two series ($r = 0.746$, $P < 0.001$).

### *Effect of chronic uremia versus chronic dietary restriction on epididymal LPL activity and role of acute fast*

Figure 1 shows that in vitro epididymal fat LPL determined after delipidation of adipose tissue by acetone and ether (AE-LPL) as expressed in terms of milliunits per gram wet weight revealed a significantly increased activity in DR rats as compared to C rats and a small decrease in U rats by comparison with C rats, which was only significant in the fed state.

The number of epididymal adipocytes observed per respective high power field under light microscopy is reported in Table 4. In the two series, a significant increase in the number of adipocytes per high power field existed for DR and U rats (not different between themselves) as compared to C rats. Furthermore, a significant inverse correlation could be demonstrated between the number of adipocytes per high power field and rat body weight at the time of sacrifice ($r = -0.719$, $P < 0.001$); all the animals were of comparable age.

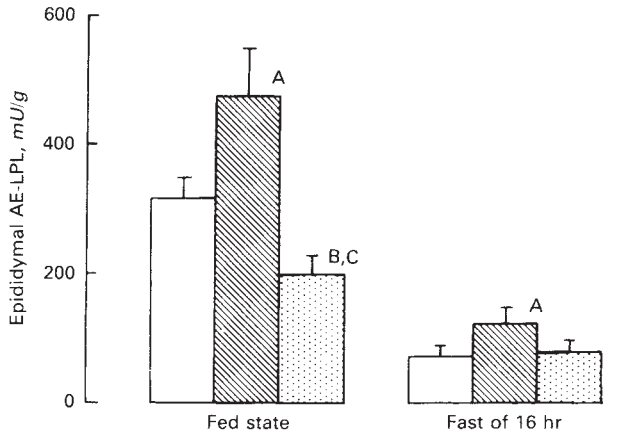


**Fig. 1.** *Epididymal AE-LPL (mU/g) of control* (□), *diet-restricted* (▨), *and uremic* (▩) *rats in the fed state* (left) *and after a 16-hr fast* (right). Each group of rats is constituted of eight animals. Results are expressed as mean + 1 SEM. A, B, and C represent a statistically significant difference when comparing diet-restricted versus control rats, uremic versus control rats, and uremic versus diet-restricted rats, respectively.

**Table 3.** Serum insulin and glucagon concentrations

| Parameter | Fasting time | Control rats ($N$ = 8) | DR rats ($N$ = 8) | Uremic rats ($N$ = 8) |
|---|---|---|---|---|
| Insulin, | 1 hr | 42.4 ± 5.2 | 38.0 ± 3.7 | 22.6 ± 1.7[b,c] |
| *mU/liter* | 16 hr | 18.5 ± 2.0 | 27.5 ± 1.9[a] | 7.1 ± 0.6[b,c] |
| Glucagon, | 1 hr | 175 ± 16 | 204 ± 10 | 306 ± 33[b] |
| *ng/liter* | 16 hr | 210 ± 17 | 214 ± 21 | 243 ± 28 |

Abbreviation: DR, diet-restricted.
[a] $P < 0.05$ or less for DR vs. Controls.
[b] $P < 0.05$ or less for Uremics vs. Controls.
[c] $P < 0.05$ or less for Uremics vs. DR.
In all other instances, $P$ is not significant.

**Table 4.** Cell number per high power field in adipose epididymal tissue

| Fasting time | Control rats ($N$ = 8) | DR rats ($N$ = 8) | Uremic rats ($N$ = 8) |
|---|---|---|---|
| 1 hr | 188 ± 19 | 297 ± 27[a] | 328 ± 15[b] |
| 16 hr | 188 ± 10 | 305 ± 17[a] | 281 ± 22[b] |

Abbreviation: DR, diet-restricted.
[a] $P < 0.05$ or less for DR vs. Controls.
[b] $P < 0.05$ or less for Uremics vs. Controls.

When considering the above results and expressing AE-LPL in terms of nanounits per $10^6$ adipocytes (instead of mU/g wet weight of fat), we could demonstrate an important decrease of the enzyme activity in U rats as compared to C or DR rats in the fed as well as in the fasted state (Fig. 2). Figure 2 also indicates that no difference was found between C and DR rats for epididymal LPL activity when expressed per cell number.

Finally, we observed a linear relation between serum insulin concentration and epididymal AE-LPL activity expressed per cell number when considering all rats of the first series ($r$ = 0.65, $P < 0.01$, Fig. 3).

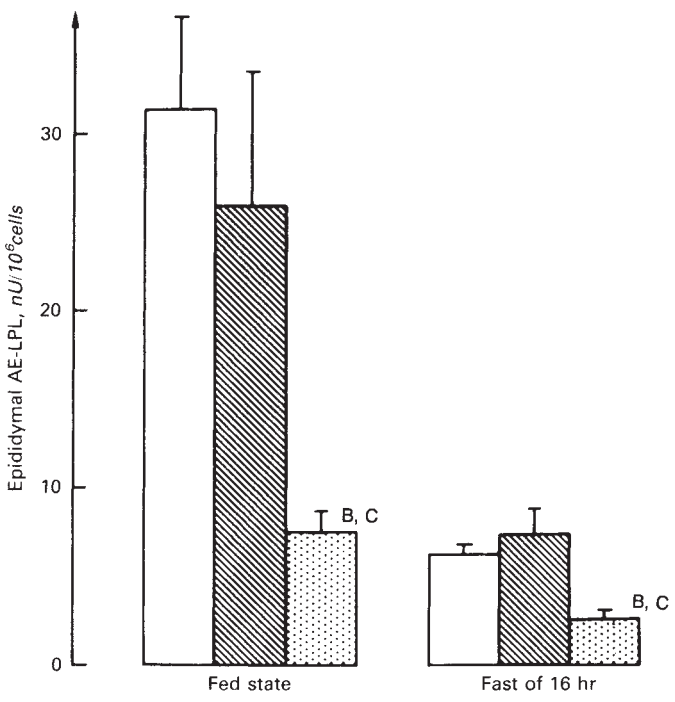


**Fig. 2.** *Epididymal AE-LPL (nU/10⁶ cells) of control* (□), *diet-restricted* (▨), *and uremic* (▩) *rats in the fed state* (left) *and after a 16-hr fast* (right). Each group of rats is constituted of eight animals. Results are expressed as mean + 1 SEM. A, B, and C represent a statistically significant difference when comparing diet-restricted versus control rats, uremic versus control rats, and uremic versus diet-restricted rats, respectively.

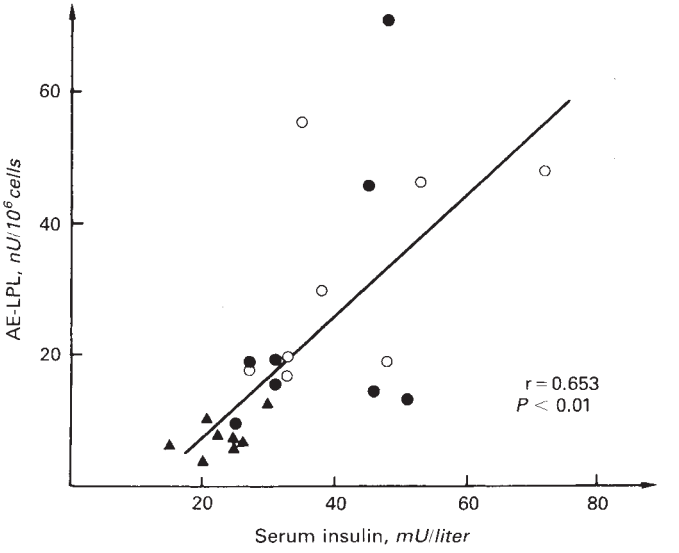


**Fig. 3.** *Relationship between serum insulin concentration (mU/liter) and AE-LPL activity* (nU/$10^6$ cells) *in eight control rats* (○), *eight diet-restricted rats* (●), *and eight uremic rats* (▲) *in the fed state.*

## Discussion

The present study confirms and extends previously reported experimental data on the hypertriglyceridemia of chronically uremic rats [21–23]. In addition, it clearly demonstrates a

deficiency of adipose tissue LPL activity at the cellular level.

In the fed state, serum TG of U rats were higher than after a 16-hr fast, indicating a probable contribution of intestinal absorption via chylomicrons. It is interesting to note that in the fed state, mean serum TG concentration and also that of TG-rich particles was lower in U (and also in DR) rats than in C rats which signifies a lesser or delayed intestinal contribution to hypertriglyceridemia in the former as compared to the latter, as already suggested by other investigators [24].

Since the increase in serum TG-rich particles during chronic renal failure is not due to hepatic overproduction [22, 25], it must be linked to their diminished catabolism as evidenced by Gregg et al [25]. This is the reason why several investigations were devoted to lipoprotein lipase, the principal enzyme implicated in TG metabolism.

Our study demonstrates that LPL activity of epididymal adipose tissue was higher in the fed state than after a 16-hr fast, which agrees with previous studies [26, 27]. DR rats again had a more marked increase in enzyme activity than C or U rats.

When examining the cells of epididymal adipose tissue of U and DR rats under the light microscope, we observed that they had a smaller size than C rats. Since the number of adipocytes as well as their size increase to a certain age [28] and then become stabilized [29], we hypothesized that in the present study the total number of adipocytes should be the same in all animal groups of comparable age but that the adipocyte size should vary according to the different metabolic (diet restriction) or pathological (uremia) conditions. In fact, the latter two conditions were associated with a decrease in adipose cell size and also in total epididymal fat mass as compared to the control state of ad-lib fed animals. Such a constellation results in an increase in the number of adipocytes per grams of tissue weight.

However, the real working possibilities of adipocytes can only be appreciated when expressing their activity either in terms of function at the cellular level or at the level of total fat mass. In the DR rats of the present study, LPL activity was significantly increased when expressed per gram of tissue weight as compared to C animals but was identical for both animal groups when expressed per number of cells. The metabolic performance of adipose tissue was thus intact in both animal groups. In contrast, LPL activity of uremic rats, when expressed per gram of tissue weight was not different from that of C rats whereas it was markedly diminished when expressed per number of cells. Thus, the metabolic performance of adipose tissue and its clearance capacity were significantly altered in the uremic state when assuming that epididymal fat was representative of total adipose tissue in those rats.

In our opinion, this notion is important since it allows reconciliation of discrepancies between several studies of the literature that could be reduced to a simple problem of expression of the results. Bagdade et al [22] expressed LPL activity per milligram of tissue and found an adipose tissue activity in uremic rats comparable to that of control rats. This finding led them to conclude erroneously that there was probably no quantitative defect of LPL activity contributing to the increase in serum TG. In humans, the only two studies that reported LPL activity of uremic adipose tissue expressed per number of cells led to the conclusion of a significantly decreased activity when compared to that of control subjects [4, 5].

Such a cellular LPL deficiency in uremic rats can alone explain the increased serum TG-rich particle concentrations. However, it does not exclude a functional abnormality of the enzyme as suggested by others [30, 31]. In addition, LPL deficiency by limiting triglyceride deposition in adipose tissue could be involved in the poor nutritional state of chronic renal failure since uremic rats had a lesser weight gain than their diet-restricted counterparts after a comparable food intake. Whether such a mechanism, as a direct or indirect consequence of the insulin deficiency state, plays an important role in uremic wasting cannot be solved, however, on the basis of the present data. Further experiments including chronic insulin supplementation and determinations of growth and cell energy regulating hormones are required to evaluate the respective roles of the different factors potentially involved in uremic malnutrition.

Concerning the orientation of energy metabolism in the uremic organism, it must be noted that all serum analyses were performed after decapitation of the animals to eliminate the influence of stress and anesthesia [32]. In the fed state the observed insulin deficiency associated with normal NEFA and increased BOB concentrations points to a preferential hepatic use of NEFA for ketone body production in U rats instead of TG synthesis since insulin regulates the activity of both pathways [33, 34]. The absence of an increase in BOB formation during prolonged fast can be explained by the reduced fat mass in uremia associated with a decreased peripheral production of NEFA as indicated by low serum NEFA concentration.

The metabolic orientation of DR rats was similar to that of C rats in the fed state and disturbed after a 16-hr fast, but in a way different from that of U rats, that is, higher serum insulin concentration and lower serum NEFA and BOB concentrations when compared to C rats. This behavior could partially be due to the difficulty to maintain DR rats within a time schedule of fast similar to that of other rats. This appears to be a severe limitation of the use of DR animals as controls when studying the utilization of energetic substrates.

The above-described metabolic reorientation of the uremic organism cannot lead to a hepatic overproduction of TG responsible of the increase in TG-rich lipoproteins. In contrast, the insulin deficiency must be at least partially responsible for the observed decrease in adipocyte LPL activity as suggested by the positive relation between AE-LPL at the cellular level and serum insulin, in line with the well-known fact that insulin stimulates LPL synthesis [26, 35–37]. Despite the fact that adipose tissue LPL represents only 54% of total body enzyme activity in fed (adult) rats and only less than 20% in starved rats [38], it is reasonable to hypothesize that not only adipose but whole body LPL activity is diminished during hypoinsulinemia leading thereby to an impaired clearance of TG-rich lipoproteins. Thus, the decrease in LPL activity should also be of utmost importance in the pathogenesis of the hypertriglyceridemia in uremia.

Whether the high circulating immunoreactive glucagon levels may in addition play a role in the hypertriglyceridemia of chronic renal failure remains speculative since in uremia much of the measured hormone may be biologically inactive [39].

In conclusion, the present study confirms the existence of an adipose tissue LPL deficiency in chronic experimental uremia at least when assuming that epididymal fat is representative of total adipose tissue of the organism. This data strongly suggest that the decreased metabolic capacities of adipose tissue con-

tribute in an important manner to the impaired catabolism of TG-rich particles in uremia. The cause of such an enzyme deficiency in uremic animals cannot be attributed to their diminished nutritional state but appears to be related to the diminution of circulating insulin. Thus, the observed disturbances of carbohydrate metabolism including disturbed levels of glucoregulatory hormones represent a key factor for the lipid anomalies of experimental chronic renal failure.

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